The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

Variant: NM_004360.4(CDH1):c.283C>T (p.Gln95Ter)

463775 (ClinVar)

Gene: CDH1 (HGNC:999)
Condition: CDH1-related diffuse gastric and lobular breast cancer (MONDO:0007648)
Inheritance Mode: Autosomal dominant inheritance
UUID: b376ba62-95aa-49c6-8b93-54ef1ce4448e
Approved on: 2018-11-21
Published on: 2018-12-07

HGVS expressions

NM_004360.4(CDH1):c.283C>T (p.Gln95Ter)
NM_004360.4:c.283C>T
NM_004360.5(CDH1):c.283C>T (p.Gln95Ter)

Pathogenic

Met criteria codes 4

PVS1 PM5_Supporting PM2_Supporting PS4_Moderate

Not Met criteria codes 22

PM3 PM4 PM1 PM6 BA1 BS2 BS4 BS3 BS1 BP5 BP7 BP2 BP3 BP1 BP4 PS2 PS1 PS3 PP2 PP3 PP1 PP4

Evidence Links 1

Expert Panel

CDH1 VCEP

Criteria Specification Information

Criteria Specification: *ClinGen CDH1 Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines Version 3.1*
Criteria Specification Approval History
Criteria Specifications for this VCEP

Evidence submitted by expert panel

CDH1 VCEP

The c.283C>T (p.Gln95*) variant is predicted to result in a premature stop codon that leads to a truncated or absent protein (PVS1, PM5_Supporting). The variant is present in <1/100,000 alleles in the gnomAD cohort. (PM2_Supporting; http://gnomad.broadinstitute.org). This variant has been reported in at least 2 families meeting HDGC clinical criteria (PS4_Moderate; PMID: 17545690, internal laboratory contributor). In summary, this variant meets criteria to be classified as pathogenic based on the ACMG/AMP criteria applied as specified by the CDH1 Variant Curation Expert Panel (Variant Interpretation Guidelines Version 3.1): PVS1, PM2_Supporting, PS4_Moderate, PM5_Supporting.

Met criteria codes

PVS1	✔	Truncation in exon 3 of 16.
PM5_Supporting	✔	Apply PM5_Supporting to nonsense/frameshift variants that are predicted/proved to undergo NMD.
PM2_Supporting	✔	Because only 1 allele in gnomAD
PS4_Moderate	✔	2 families - Family 1 (Excel document). Observed in an individual with DGC at 39yo, 2 paternal aunts with GC (not known if they are carriers). Family 2: PMID: 17545690, one family with 7 GC, 2 confirmed DGC. Table. 2. Lists family F1 with 7GC in the family 2 confirmed as DGC. Age range of GC diagnosis 39 to 76. No LBC reported. PubMed:17545690

Not Met criteria codes

PM3	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM4	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM1	✖	Truncating variant. PMID: 18427545 supports PTC.
PM6	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BA1	✖	Because only 1 allele in gnomAD
BS2	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS4	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

BS3	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS1	ℹ	✖	Because only 1 allele in gnomAD
BP5	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP7	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP2	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP3		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP1		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP4	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS2	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS1		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS3	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP2		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP3	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP1	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP4		✖	Table. 2. Lists family F1 with 7GC in the family 2 confirmed as DGC. Age range of GC diagnosis 39 to 76. No LBC reported. **PubMed:17545690**

Curation History

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